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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/417,478	10/13/1999	JOHN MCCAFFERTY	05569.0004.DVUS07	8812

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EXAMINER
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LIU, SUE XU

ART UNIT	PAPER NUMBER
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1639

MAIL DATE	DELIVERY MODE
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05/17/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

Application No.

09/417,478

Applicant(s)

MCCAFFERTY ET AL.

Examiner

Sue Liu

Art Unit

1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 21 March 2007.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 44-53 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 44-53 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/21/07 has been entered.

### ***Claim Status***

2. Claims 44-53 are currently pending;
- Claims 44-47 and 50-53 have been amended as filed on 3/21/07.
- Claims 44-53 are being examined in this application.

### ***Priority***

3. This application appears to be a Divisional of U.S. Patent Application Nos. 08/484,893 (filed 6/07/1995), which is now a US PATENT, 6,172,197, which is a CON of 07/971,857 (filed 1/8/1993; now US PAT 5,969,108), which is a 371 of PCT/GB91/01134 (filed on 7/10/1991).

Art Unit: 1639

***Drawings***

4. The following regarding informal drawings are noted in the previous office action (11/20/2000; pg 2):

This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Applicant is invited to notice that boxes 2, 6 and 12 were checked by the draftsman in PTO 948. Applicant is encouraged to amend the specification so that the description of renumbered figure corresponds to the renumbered figures.

Applicant's request of holding the formal drawing requirements in abeyance until allowance is acknowledged.

***Specification***

5. Applicant's amendments to the specification filed on 3/21/07 is acknowledged and entered in the file.

Applicants are invited to update the status of the parent applications in the first line of the specification.

***Claim Rejections Withdrawn***

6. Upon further consideration and in light of applicants' arguments and amendments to the claims, the following claim rejections are withdrawn:

A.) Claims 44 and 46, as amended or originally filed, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such

Art Unit: 1639

a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (Written Description Rejection).

B.) Claims 44 and 45, as amended or originally filed, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for recombinant cells harboring library of specific binding pair member comprising single chain antibody, does not reasonably provide enablement for recombinant cells harboring any other specific binding pair members. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. (Scope of Enablement Rejection).

C.) Claims 44-53 as amended are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

However, new rejections under 35 U.S.C. 112, second paragraph are formulated below. Applicant's relevant argument pertaining to the rejection under 35 U.S.C. 112, second paragraph, are also answered below.

### **New Claim Rejections**

#### ***Claim Rejections - 35 USC § 112***

#### **Second paragraph of 35 U.S.C. 112**

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

Art Unit: 1639

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 44-53 as amended are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 44 recites the limitation "said bacteriophage particle's associated displayed member" in line 13. There is insufficient antecedent basis for this limitation in the claim. In addition, the said phrase "said bacteriophage particle's associated displayed member" is unclear and can be interpreted variously. For example, the claim language can be interpreted to mean that the genetic material of the "bacteriophage particle" encodes a member that is "associated" with the "displayed member", i.e. the "complementary specific binding pair member" of the displayed "one member of a specific binding pair". That is to say both members of the "specific binding pair" are encoded in the genetic material of the phage particle. However, applicants have clearly stated in the Reply (entered 3/21/07, p. 13) that only "one member" of the specific binding pair is intended by the claim language. Therefore, the claim language is unclear and renders the instant claims indefinite.

#### Discussion and Answer to Argument

9. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in *italic*):

*Applicants assert the claim amendments have obviated the previous rejection under 35 USC 112, 2<sup>nd</sup> paragraph.*

Art Unit: 1639

However, the claim amendment has elicited new issues as discussed above.

Applicants are respectively directed to the above rejection for a detailed discussion.

***Claim Rejections - 35 USC § 102***

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(Note: the instant claim numbers are in bold font.)

*Smith et al*

11. Claims 44 and 45 are rejected under **35 U.S.C. 102(b)** as being anticipated by Smith et al (Science. Vol. 228: 1315-1317; 6/14/1985; cited in IDS entered 2/1/2000).

The instant claims recite a recombinant host cells each of which harbors a nucleic acid fragment encoding one member of a specific binding pair whereby the host cells collectively harbor a library of nucleic acid fragments comprising fragments encoding a genetically diverse population of specific binding pair members, each member of a specific binding pair being expressed as a fusion with a gene III coat protein surface component of a filamentous bacteriophage so that each said member of a specific binding pair comprises a binding domain for its complementary specific binding pair member and is displayed on the surface of bacteriophage particles, and genetic material of each said bacteriophage particle encodes said bacteriophage particle's associated displayed member of a specific binding pair, said genetic material being a phagemid genome which is plasmid nucleic acid containing a single stranded phage replication origin and a

Art Unit: 1639

nucleotide sequence encoding said fusion and wherein said genetic material is packaged into particles by a helper phage whereby each particle has a coat partially derived from the helper phage and partly from said fusion.

Smith et al, throughout the publication, teach phage displaying antigens, which are screened for specific binding antibodies (Abstract).

The reference teaches inserting a nucleic acid encoding for an antigen (such as a fragment of a endonuclease) (p. 1315, col. 2, para 1), which the antigen reads on the "one member of a specific binding pair" of **clm 44** because the antigen binds to a specific antibody (i.e. the other member of the "specific binding pair").

The reference teaches using filamentous phage and fusing the antigen with the Gene III coat protein (p. 1315, cols. 1-2), which reads on the phage and the gene III coat protein of **clm 44**.

The reference also teaches using host cells to grow the phage particles (cols. 1-3), which reads on the "recombinant host cells" of **clm 44**.

The reference also teaches using the genome of phage fl (col. 1, last para), which reads on the phagemid genome of **clm 44**.

The reference also teaches mutating the insertions (col. 2), which reads on the limitation of **clm 45**.

Parmley et al

12. Claims 44 and 45 are rejected under **35 U.S.C. 102(b)** as being anticipated by Parmley et al (Gene. Vol. 73: 305-318; 1988; cited in IDS entered 2/1/2000).



Art Unit: 1639

Parmley et al, throughout the publication, teach phage displaying antigens, which are screened for specific binding antibodies (Abstract).

The reference teaches inserting a nucleic acid encoding for an antigen (such as fragments of  $\beta$ -gal protein) (e.g. p. 307, col. 1, para 1), which the antigen reads on the "one member of a specific binding pair" of **clm 44** because the antigen binds to a specific antibody (i.e. the other member of the "specific binding pair").

The reference teaches using filamentous phage and fusing the antigen with the Gene III coat protein (e.g. p. 310), which reads on the phage and the gene III coat protein of **clm 44**.

The reference also teaches using host cells to grow the phage particles (e.g. p. 306, col. 2), which reads on the "recombinant host cells" of **clm 44**.

The reference also teaches using the genome of phage (e.g. p. 306; pp. 310-311), which reads on the phagemid genome of **clm 44**.

The reference also teaches mutating the insertions (e.g. p.307), which reads on the limitation of **clm 45**.

Ladner ('409)

13. Claims 44 and 45 are rejected under **35 U.S.C. 102(b)** as being anticipated by Ladner et al (US 5,223,409; filed 3/1/1991; priority date: 9/2/1988; cited in IDS filed 2/1/2001).

Ladner et al, throughout the patent, teach using phage display to express binding domains (Abstract).

Art Unit: 1639

The reference teaches inserting a nucleic acid encoding for a binding domain (e.g. claim 1), which the antigen reads on the "one member of a specific binding pair" of **clm 44**.

The reference teaches using filamentous phage and fusing the antigen with the Gene III coat protein (e.g. cols. 5-6), which reads on the phage and the gene III coat protein of **clm 44**.

The reference also teaches using host cells to grow the phage particles (e.g. col. 6, lines 1+), which reads on the "recombinant host cells" of **clm 44**.

The reference also teaches using the genome of phage (e.g. col. 54), which reads on the phagemid genome of **clm 44**.

The reference also teaches mutating the insertions (e.g. cols. 31-32), which reads on the limitation of **clm 45**.

The reference also teaches displaying single chain antibodies using phage display (e.g. cols. 6-7), which reads on the immunoglobulin binding domains and the scFv of **clms 46-53**.

### ***Claim Rejections - 35 USC § 103***

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

*Parmley et al and Ladner (WO)*

15. Claims 8-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parmley et al (Gene. Vol. 73: 305-318; 1988; cited in IDS entered 2/1/2000), in view of Ladner et al (WO 88/06630; 9/7/1988; cited in IDS entered 2/1/2000).

Parmley et al, throughout the publication, teach using phage particles to display protein fragments of various sizes (as discussed above).

Parmley et al do not explicitly teach using phage particles to display antibody (or immunoglobulin "binding domains", as recited in **clms 46-49**, and more specifically, scFv molecules as recited in **clms 50-53**.

However, Ladner et al, throughout the publication, teach using phage (lamda phage) to display antibody fragments such as single chain antibodies (e.g. Abstract, pp.2-3): The reference teaches generating a large repertoire of genes encoding for single chain antibodies and displaying the antibodies on the surface of the phage (e.g. p. 4; Figure 3).

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to generate recombinant cells comprising phage display particles displaying "binding domains" of antibodies or immunoglobulins, or single chain antibodies.

A person of ordinary skill in the art would have been motivated at the time of the invention to use filamentous phage display method to generate recombinant cells comprising antibody binding domains or single chain antibodies, because phage display allow efficient screening of large library of proteins, as taught Parmley et al (p. 316), and phage displaying antibodies would have the advantages such as creating a diverse population of antibodies, as taught by Ladner et al (e.g. p. 4).

Art Unit: 1639

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications, because Parmley et al have shown that different proteins with different sequences and/or sizes can be successfully displayed in phage, and Ladner et al have shown that antibodies can be successfully displayed in phage, as discussed above.

### *Conclusion*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JON EPPERSON  
PRIMARY EXAMINER



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Art Unit 1639  
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